PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P450869 KJR	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
International Application No. PCT/NZ01/00228	International Filing Date *(day/month/year)* 16 October 2001	Priority Date *(day/month/year)* 17 October 2000

International Patent Classification (IPC) or national classification and IPC

Int. Cl.[7] A61K 35/39; A61P 3/10

Applicant

DIATRANZ LIMITED et al

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheet(s).

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of the report
10 April 2002	16 December 2002
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer **JULIE CAIRNDUFF** Telephone No. (02) 6283 2545

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/NZ01/00228

I. Basis of the report

1. With regard to the elements of the international application:*

☐ the international application as originally filed.

☒ the description, pages **1, 3, 4, 5, 7, 9 to 34** as originally filed,

pages , filed with the demand,

pages **6 and 8** received on **11 October 2002** with the letter of **10 October 2002**

pages **2** received on **29 November 2002** with the letter of **25 November 2002**

☒ the claims, pages **35 to 37** as originally filed,

pages , as amended (together with any statement) under Article 19,

pages , filed with the demand,

pages **38 to 41** received on **11 October 2002** with the letter of **10 October 2002**

☒ the drawings, pages **1/10 to 10/10** as originally filed,

pages , filed with the demand,

pages , received on with the letter of

☐ the sequence listing part of the description:

pages , as originally filed

pages , filed with the demand

pages , received on with the letter of

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages

☐ the claims, Nos.

☐ the drawings, sheets/fig.

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report*

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	**1-63**	**YES**
	Claims		**NO**
Inventive step (IS)	Claims	**1-63**	**YES**
	Claims		**NO**
Industrial applicability (IA)	Claims	**1-63**	**YES**
	Claims		**NO**

2. Citations and explanations (Rule 70.7)

Citations

D1: London, N.J. et al. (1990) Transplantation 49(6): 1109-13;

D2: Selawry, H.P. et al. (1993) Cell Transplantation 2: 123-129;

D3: Korbutt, G.S. et al. (1997) Diabetes 46: 317-322;

D4: Rayat, G.R. et al. (1999) Annals of the New York Academy of Sciences 875: 175-188;

D5: Suaraz-Pinzon, W. et al. (2000) Diabetes 49: 1810-1818;

D6: Luca, G. et al. (2000) Journal of Investigative Medicine 48(6): 441-448;

D7: Selawry, H. P. et al. (1996) Cell Transplantation 5(5): 517-524;

D8: Calafiore, R. et al. (1999) Annals of the New York Academy of Sciences 875: 219-232;

D9: AU 81864/98 (DIANTRANZ LIMITED) 11 March 1999; and

D10: US 6146653 (DIATRANZ LIMITED) 14 November 2000.

New Citation

D11: AU 18057/00 (UNIVERSIDAD NACIONAL AUTONOMA DE MEXICO) 22 June 2000.

Novelty and Inventive Step

D1 discloses collagenase digestion of human pancreatic tissue, with treatment of the lysate with minimum essential medium containing nicotinamide supplemented with newborn calf serum. It does not disclose xenotransplantation with or without implants or the use of Sertoli cells. D2 refers to allotransplantation of human islet cells associated with Sertoli cells. The islet cells of D2 are prepared by the method described in D1 and transplantation of the cells was without encapsulation. D3 discloses allotransplantation of rat islet cells associated with Sertoli cells prepared by collagenase digestion and treated with non-human mammalian sera. D4 discusses xenotransplantation of neonatal porcine islet cells to mice, associated with Sertoli cells. However it the effect of cotransplantation is not known and is still being investigated.

Continued in Supplemental Box II

Supplemental Box I

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Box I

Rule 67 lists the subject matter which under Article 34(4)(a)(i) an international preliminary examination is not required to be carried out. At item (iv) it specifies methods for treatment of the human or animal body by surgery or therapy, as well as diagnostic methods, as such matter. However the agreement between WIPO and Australia further qualifies this by excepting from exclusion any subject matter which is examined under national grant procedures. Claims 41 to 50 have nonetheless been considered because the identified subject matter does not contravene Australian law.

Supplemental Box II

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of V

D5 describes transplantation of Sertoli cells and islet cells in mice without encapsulation. Transforming growth factor β1 abrogated the protective effect of the Sertoli cells. D6 discloses the *in vitro* culture of rat Sertøli cells with rat islet cells and xenotransplantation of the culture using an alignate/poly-1-ornithine microcapsule into mice.

D8 discloses allografts of canine islet cells in low volume capsules with reduced immune attack of the grafts. Porcine islets, collagenase extraction and Sertoli cells were not described. D9 and D10 disclose xenografts of collegenase extracted, nicotinamide treated neonatal porcine islet cells into mice and humans. There is no disclosure of the use of Sertoli cells, trauma protecting agents, any particular mammalian albumin or encapsulation of transplanted cells.

In light of D1 to D6 and D8 to 10, none of these documents disclose all the essential features of claims 1 to 63. In particular a method to prepare a xenotransplantable porcine islet preparation the use of porcine islet cells, extraction of islet cells using collagenase and the association of islet cells with Sertoli cells; a method of prepare an implantable device containing a xenotransplantable porcine islet preparation; implantable devices per se; and methods of treatment. Therefore the subject matter of claims 1 to 63 is new and inventive and meets the criteria set forth in PCT Article 33(2) for novelty and inventive step.

D7 is considered to be the closest related art. This document refers to the extraction of neonatal porcine islet cells with collagenase, treatment with media containing nicotinamide and culture in a medium containing inactivated horse serum. Islet cells were cryopreserved and the effect of Sertoli cells on survival rate at thawing was measured. Enhanced islet cell survival and response to glucose was noted in the presence of Sertoli cells. It is concluded in this document that co-culture of islet cells with Sertoli cells significantly increased islet yield and beta cell responsiveness to glucose. D7 suggests that there have been studies regarding the successful survival of piglet islets in vivo following transplantation into diabetic rats, however no evidence was published at the priority date of the present application and therefore no instructions for the skilled worker to follow. Claims 1 to 63 are therefore novel and inventive in light of this document because it does not disclose the specific steps of the method of preparing a xenotransplantable porcine islet preparation as described in claim 1, the method of preparing an implantable device containing a xenotransplantable porcine islet preparation as described in claims 17 and 51; implantable devices per se as described in claims 31 and 36, and methods of treatment using such implantable devices as described in claim 42.

With reference to D11, this document discloses a device which is to be used for the implantation of cells producing biological factors in the treatment of diseases such as diabetes mellitus. The device possesses a porous intermediate section acting as a reservoir for neovascularized cells and a plunger mechanism. The device enables the formation of fibrocollagen tubes in a patient and allows a controlled dosage of the cells to be delivered to the patient. In particular the example provided in D11 refers to a transplant of islet cells to rats with induced diabetes whereby the rats showed a significant decrease in glucose levels. However there is no reference to the feature of co-culture Sertoli cells, which is an essential feature of the invention. Consequently claims 1 to 63 are novel and inventive and meet the criteria set forth in PCT Article 33(2) for novelty and inventive step.